REMARKS

Claims 1, 3, 5, 13, 14, 16, 26, 31, 33, 35, 42, 75, 81, 83, 84, 85 and 88 have been amended. No new matter has been added. Support for the claim amendments may be found throughout the specification and in the claims as filed. Claims 4, 14-25, 34 and 46-74 have been cancelled without prejudice. Applicants reserve the right to prosecute the subject matter of those claims in a continuing application

Claims 1-3, 5-13, 26-33 and 75-89 are pending.

CLAIM OBJECTION

The Examiner has objected to claims 1, 5, 31, 47 and 66 due to typographical errors. See Office Action at p. 2. Claims 47 and 66 have been cancelled thus rendering this objection moot with respect to those claims. Applicants have amended claims 1, 5, 31, 47 and 66 to correct the typographical errors as outlined by the Examiner. Applicants respectfully request the withdrawal of this claim objection.

CLAIM REJECTIONS

Rejection of claims under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 1-25 under 35 U.S.C. § 112, second paragraph, as being indefinite. See Office Action at p. 2. Specifically, the Examiner contends that "[t]he term 'low' in claims 1 and 14 is a relative term which renders the claim indefinite." Id. Applicants respectfully traverse this rejection. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 14-25 have been cancelled thus rendering this rejection moot with respect to those claims. Claims 2-13 depend from independent claim 1.

The term "low immunogenicity" is explained on p. 6, lines 30-32 of the specification, as "the inability of the natural molecule to elicit a strong immune response resulting in the production of high affinity antibodies." The specification also describes reasons why certain antigens have low immunogenicity on page 12, line 6 to page 13, line 6. Antigens with low immunogenicity are also listed on Table 1 of the specification. Thus Applicants believe the phrase "low" as it applies to immunogenicity is not indefinite. A person of skill in the art, in

light of the specification, would understand the meaning of the phrase "low" as it applies to immunogenicity.

Applicants thus respectfully request reconsideration and the withdrawal of this rejection.

Rejection of claims under 35 U.S.C. § 112, first paragraph

Written Description

The Examiner has rejected claims 73 and 83 under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement. See Office Action at p. 3. Specifically, the Examiner contends that"[t]he claims encompass[] a broad genus of 'reagents' that would include binding agents such as antibodies, enzymes, protein ligands or chemical ligands which could be isolated from protein libraries and small molecule chemical libraries." Id. Not in acquiescence to this rejection but in an effort to expedite prosecution, claim 73 has been cancelled thus rendering this rejection moot with respect to this claim.

Applicants have amended claim 83 to clarify that the reagent that specifically detects Prior protein is the monoclonal antibodies produced by the method described in claim 75. Applicants submit that the specification sufficiently describes the invention in full, clear, concise and exact terms. As such, Applicants respectfully request reconsideration and the withdrawal of this rejection.

Enablement

The Examiner has rejected claims 1-3, 5-16, 18-33, 36-53, 56-65, 67, 74-80, 82, 84-84 and 89 under 35 U.S.C. § 112, first paragraph for lack of enablement. See Office Action at p. 4. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 14-16, 18-25, 46-53, 56-65, 67 and 74 have been cancelled thus rendering this rejection moot with respect to those claims.

Specifically, the Examiner contends that "the specification, while being enabling for the method of claims 1, 26, 75, 84 and 85, wherein the animal is a mammal and the hybridoma is produced by a fusion with a non-human immortalized mammalian cell, does not reasonably provide enablement for the method of claims 1, 26, 75, 84 and 85, wherein the animal is not a

mammal, or wherein the fusion to provide the hybridoma is with a human immortalized cell, or wherein the screening for specificity is based on a 'protein A' assay." Id.

With respect to remaining pending claims 11 and 63, the Examiner contends that "[t]he art teaches that chimeric hybridomas made by fusions of human B cells with mouse immortal cells are rare and that most such hybrids, with rare exceptions, tend to be highly unstable due to loss of human chromosomes ...." See Office Action at p. 4. The Examiner then states that "[i]t is reasonable to conclude that not all combinations of activated B cell and immortalized cell will produce a stable chimeric hybridoma secreting antibody" and that "[t]he specification fails to address this unreliability in the art." See Office Action at p. 4-5. As such, the Examiner contends that "one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to carry out the claimed methods using an immortalized human cell as the fusion partner for an animal B cell." See Office Action at p. 5. To support the Examiner's contentions, the Examiner has cited two references, namely, Kaplan, 'Monoclonal Human Antibodies,' In: Monoclonal Antibodies in Clinical Medicine, McMichael and Favre, Eds., 1982, p. 18 and Milstein, 'Monoclonal Antibodies from Hybrid Myelomas,' In: Monoclonal Antibodies in Clinical Medicine, McMichael and Favre, Eds., 1982, p. 9. See Office Action at p. 4. Applicants respectfully traverse this argument as the references cited are not representative of the amount of knowledge in the art of the art at the time this application was filed.

Additionally, MPEP 2164 states that

> [t]he purpose of the requirement that the specification describe the invention in such terms that one skilled in the art can make and use the claimed invention is to ensure that the invention is communicated to the interested public in a meaningful way. The information contained in the disclosure of an application must be sufficient to inform those skilled in the relevant art how to both make and use the claimed invention. >However, to comply with 35 U.S.C. 112, first paragraph, ***it is not necessary to "enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim limitation to that effect."*** *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1338, 68 USPQ2d 1940, 1944 (Fed. Cir. 2003) (an invention directed to a general system to improve the cleaning process for semiconductor wafers was enabled by a disclosure showing improvements in the overall system).< Detailed procedures for making and using the invention may not be necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention.

(emphasis added by Applicants). Thus, all the law requires is that a patent applicant provide a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of the claims. The specification has informed and demonstrated to a person having ordinary skill in the art how to use the invention commensurate in scope with the claims. Accordingly, the specification adequately enables a method of producing antibodies specific to an antigen of low immunogenicity and a composition of monoclonal antibodies produced by such a method.

With respect to remaining pending claim 13, the Examiner contends that those claims are not enabled as "[o]ne of skill in the art would be subject to undue experimentation [in] order to screen the secreted antibodies from the hybridomas using a protein A assay for IgG." See Office Action at p. 5. Applicants respectfully traverse this rejection. A person of skill in the art would understand that "protein A assay" does not simply refer to screening antibodies from the hybridomas for IgG. One of skill in the art would consider utilizing protein A in a number of assays to screen for specificity of a monoclonal antibody to an antigen. As stated in MPEP 2164.01, "[a] patent need not teach, and preferably omits, what is well known in the art." Applicants thus believe that Applicants have informed and demonstrated to a person having ordinary skill in the art how to use the invention commensurate in scope with the claims. Applicants respectfully request reconsideration and withdrawal of this rejection.

With respect to claims 1-3, 5-16, 18-33, 36-53, 56-65, 74-80, 82, 84-87 and 89, the Examiner has rejected the claims as being "broadly drawn to include the immunization of animals which are not mammals ...." See Office Action at p. 5. In an effort to expedite prosecution and not in acquiescence to the rejection, Applicants have amended independent claims 1, 75, 84 and 85 to clarify that the animal is a mammal. Applicants thus believe that Applicants have informed and demonstrated to a person having ordinary skill in the art how to use the invention commensurate in scope with the claims. Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of claims under 35 U.S.C. § 102(b)

Seiki

The Examiner has rejected claims 1, 3, 4, 6, 8-10, 13-25, 85, 88 and 89 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,191,255 to Seiki et al. ("Seiki"). See Office Action at p. 6. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 14-25 have been cancelled thus rendering this rejection moot with respect to those claims. Claims 3, 6, 8-10, 13 depend from independent claim 1. Claims 88 and 89 depend from independent claim 85. Claims 4 and 17 have been cancelled thus rendering this rejection moot with respect to those claims.

Claim 1 relates to a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including a) conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein, b) immunizing a mammal with the conjugated antigen, c) harvesting B cells from the mammal, d) creating hybridomas from the harvested B cells, e) screening the hybridomas for specificity to the native antigen.

Claim 85 relates to a method of producing monoclonal antibodies specific to matrix metalloprotease 3 including a) conjugating the matrix metalloprotease 3 chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein, b) immunizing a mammal with the conjugated antigen, c) harvesting B cells from the mammal, d) creating a hybridoma from the harvested B cells, and e) screening the hybridomas for specificity to the native matrix metalloprotease 3.

Seiki describes methods of making a monoclonal antibody to human MT-MMP-3 and further describes that fragment so MT-MMP-3 "be coupled with various carrier proteins via suitable coupling agents to form immunogenic conjugates such as hapten-proteins." See col. 18, lines 27-36 and col. 18, line 63 to col. 19, line 3. Seiki further states that "[t]he carrier proteins include keyhole limpet haemocyanin (KLH), bovine serum albumin (BSA), ovalbumin, globulin, polypeptides such as polylysine, bacterial components such as BCG or the like." See col. 19, lines 15-18. Seiki does not describe a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Seiki additionally does not describe a method of producing monoclonal antibodies specific to matrix

metalloprotease 3 including conjugating the matrix metalloprotease 3 chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 85.

As such, independent claims 1 and 85 and dependent claims thereof are not anticipated by Seiki. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Cashman

The Examiner has rejected claims 1, 3, 4, 8-10, 13-25, 75 and 81-83 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 7,041,807 to Cashman et al. ("Cashman"). See Office Action at p. 8. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 4 and 14-25 have been cancelled thus rendering this rejection moot with respect to those claims. Claims 3, 8-10 and 13 depend from independent claim 1. Claims 81-83 depend from independent claim 75. Claim 83 is an independent claim.

Cashman describes "antibodies specific for PrP^{Sc} and diagnostic, therapeutic, and decontamination uses thereof." See Abstract. Cashman further describes:

> [i]n addition to the goat polyclonal antibody generation, monoclonal antibodies against the same PrP^{Sc} -specific epitope were also generated, but with a derivative of the original antigen in which multiples of the original YYR peptide were linked together into one contiguous sequence. YYRRYYRYY (SEQ ID NO: 31) was synthesized in an attempt to increase the number of YYR epitopes in the peptide sequence, and to increase the chance of tyrosine stacking and/or frequency of pi-stacking. Moreover, one of the YYR sequences in the prion protein is preceded by an arginine in the five species of interest (FIG. 2). The YYRRYYRYY peptide was linked to KLH and mice were subsequently immunized with the antigen.

See col. 13, lines 5-17. Cashman does not describe a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Cashman further does not describe a method of producing monoclonal antibodies specific to a Prion protein peptide including conjugating the Prion protein peptide chemically to a carrier molecule wherein the carrier molecule is HSP70 and wherein the prion protein peptide is selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 9 as described in claim 75.

As such, independent claims 1 and 75 and dependent claims thereof are not anticipated by Cashman. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Korth

The Examiner has rejected claims 13-25[1] and 83 under 35 U.S.C. § 102(b) as being anticipated by Korth et al., *Nature*, Vol. 390, pp. 74-77 (1997) ("Korth"). See Office Action at p. 9. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 14-25 have been cancelled thus rendering this rejection moot with respect to those claims. Claim 13 depends from independent claim 1. Claim 83 depends from independent claim 75.

Korth describes "a monoclonal antibody, 15B3, that can discriminate between the normal and disease-specific forms of PrP." See Abstract. Korth further describes immunizing PrP-null mice with full-length recombinant bovine PrP. See p. 74. Korth does not describe a kit for determining if a subject is at risk for developing spongiform encephalopathy that includes monoclonal antibodies wherein the monoclonal antibodies are produced by conjugating the Prion protein peptide chemically to a carrier molecule wherein the carrier molecule is HSP70 and wherein the prion protein peptide is selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 9 as described in claim 75.

As such, independent claim 75 and dependent claims thereof are not anticipated by Korth. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Mathur

The Examiner has rejected claims 66, 67, 68, 73 and 74 under 35 U.S.C. § 102(b) as being anticipated by Mathur et al., *American Journal of Reproductive Immunology*, Vol. 46, pp. 280-297 (2001) ("Mathur"). See Office Action at p. 9. Not in acquiescence to this rejection but in an effort to expedite prosecution, Applicants have cancelled claims 66, 67, 68, 73 and 74 thus rendering this rejection moot with respect to those claims. Applicants respectfully request the withdrawal of this rejection.

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[1] Applicants believe that the Examiner intended to reject claims 14-25 and 83 as the Examiner does not provide any reasons why claim 13 is included in the § 102(b) rejection over Korth on page 9 of the Office Action. Applicants respectfully request clarification of this rejection.

Zwerschke

The Examiner has rejected claim 73 under 35 U.S.C. § 102(e) as being anticipated by WO 2003/080669 to Zwerschke et al. ("Zwerschke"). See Office Action at p. 10. Not in acquiescence to this rejection but in an effort to expedite prosecution, Applicants have cancelled claim 73 thus rendering this rejection moot with respect to this claim. Applicants respectfully request the withdrawal of this rejection.

Zatsepina

The Examiner has rejected claims 14-25, 46, 47, 51-65, 73 and 74 under 35 U.S.C. § 102(e) as being anticipated by Zatsepina et al., *Oncogene*, Vol. 14, pp. 1137-1145 (1997) ("Zatsepina"). Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 14-25, 46, 47, 51-65, 73 and 74 have been cancelled thus rendering this rejection moot with respect to those claims. Applicants respectfully request the withdrawal of this rejection.

Rejection of claims under 35 U.S.C. § 103

Cashman and Lawrence

The Examiner has rejected claims 1, 3, 4, 8-10, 75, 76 and 81-83 under 35 U.S.C. § 103(a) as being unpatentable over Cashman in view of U.S. Patent No. 4,859,613 to Lawrence ("Lawrence"). See Office Action at p. 11. Claim 4 has been cancelled thus rendering this rejection moot with respect to this claim. Claims 3 and 8-10 depend from independent claim 1. Claims 76 and 81-83 depend from independent claim 75.

As previously described, Cashman does not describe a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Cashman further does not describe a method of producing monoclonal antibodies specific to a Prion protein peptide including conjugating the Prion protein peptide chemically to a carrier molecule wherein the carrier molecule is HSP70 and wherein the prion protein peptide is selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 9 as described in claim 75.

Cashman does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Cashman also does not teach or suggest a method of producing monoclonal antibodies specific to a Prion protein peptide including conjugating the Prion protein peptide chemically to a carrier molecule wherein the carrier molecule is HSP70 and wherein the prion protein peptide is selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 9 as described in claim 75.

These defects are not remedied by Lawrence. Lawrence describes "[m]onoclonal antibodies specifically immunologically reactive to thiol-modified glutathione and hybridoma cell lines producing such monoclonal antibodies." See Abstract. Lawrence also describes "[a] method of producing antibodies specifically immunologically reactive with reduced glutathione by immunizing an animal using a thiol-modified glutathione, for example, a glutathione-N-ethylmaleimide-keyhole limpet hemocyanin conjugate." See Abstract. Lawrence does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Lawrence also does not teach or suggest a method of producing monoclonal antibodies specific to a Prion protein peptide including conjugating the Prion protein peptide chemically to a carrier molecule wherein the carrier molecule is HSP70 and wherein the prion protein peptide is selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 9 as described in claim 75.

Accordingly, claims 1 and 75 and dependent claims thereof, are patentable over the combination of Cashman and Lawrence for at least the reasons described above. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Seiki and Lawrence

The Examiner has rejected claims 1, 3, 4, 8-10, 13, 14, 16-19, 21, 22, 25, 85, 86, 88 and 89 under 35 U.S.C. § 103(a) as being unpatentable over Seiki in view of Lawrence. See Office Action at p. 12. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 4, 14, 16-19, 21, 22 and 25 have been cancelled thus rendering this rejection moot with

respect to this claim. Claims 3, 8-10 and 13 depend from independent claim 1. Claims 86, 88 and 89 depend from independent claim 85.

As previously explained, Seiki does not describe a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Seiki additionally does not describe a method of producing monoclonal antibodies specific to matrix metalloprotease 3 including conjugating the matrix metalloprotease 3 chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 85.

Seiki further does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Seiki also does not teach or suggest a method of producing monoclonal antibodies specific to matrix metalloprotease 3 including conjugating the matrix metalloprotease 3 chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 85.

These defects are not remedied by Lawrence. Lawrence describes "[m]onoclonal antibodies specifically immunologically reactive to thiol-modified glutathione and hybridoma cell lines producing such monoclonal antibodies." See Abstract. Lawrence also describes "[a] method of producing antibodies specifically immunologically reactive with reduced glutathione by immunizing an animal using a thiol-modified glutathione, for example, a glutathione-N-ethylmaleimide-keyhole limpet hemocyanin conjugate." See Abstract. Lawrence further does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Lawrence also does not teach or suggest a method of producing monoclonal antibodies specific to matrix metalloprotease 3 including conjugating the matrix metalloprotease 3 chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 85.

Accordingly, claims 1 and 85 and dependent claims thereof, are patentable over the combination of Seiki and Lawrence for at least the reasons described above. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Seiki and Maurer

The Examiner has rejected claims 1, 3-6, 8-10, 13-25, 85, 88 and 89 under 35 U.S.C. § 103(a) as being unpatentable over Seiki in view of Maurer and Callahan, *Methods in Enzymology*, Vol. 70A, pp. 49-70 (1980) ("Maurer"). See Office Action at p. 12. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 4 and 14-25 have been cancelled thus rendering this rejection moot with respect to those claims. Claims 3, 5-6, 8-10 and 13 depend from independent claim 1. Claims 88 and 89 depend from independent claim 85.

As previously described, Seiki does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Seiki also does not teach or suggest a method of producing monoclonal antibodies specific to matrix metalloprotease 3 including conjugating the matrix metalloprotease 3 chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 85.

These defects are not remedied by Maurer. Maurer describes "techniques that have become available for producing antibody ...." See p. 49. Maurer does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Maurer also does not teach or suggest a method of producing monoclonal antibodies specific to matrix metalloprotease 3 including conjugating the matrix metalloprotease 3 chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 85.

Accordingly, claims 1 and 85 and dependent claims thereof, are patentable over the combination of Seiki and Maurer for at least the reasons described above. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Seiki and Milstein

The Examiner has rejected claims 1, 3, 4, 6, 8-10, 12-14, 16-19, 21, 22, 24, 25, 85, 88 and 89 under 35 U.S.C. § 103(a) as being unpatentable over Seiki in view of Milstein, "Monoclonal Antibodies from Hybrid Myelomas," *In: Monoclonal Antibodies in Clinical Medicine,* McMichael and Favre, Eds, p. 9 (1982) ("Milstein"). See Office Action at p. 13. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 4, 16-19, 21, 22, 24 and 25 have been cancelled thus rendering this rejection moot with respect to those claims. Claims 3, 6, 8-10 and 12-13 depend from independent claim 1. Claims 88 and 89 depend from independent claim 85.

As previously described, Seiki does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Seiki also does not teach or suggest a method of producing monoclonal antibodies specific to matrix metalloprotease 3 including conjugating the matrix metalloprotease 3 chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 85.

These defects are not remedied by Milstein. As explained by the Examiner, Milstein describes "that hybridomas can be made by fusing rat or mouse spleen cells with rat myeloma cells." See Office Action at p. 13. Milstein does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Milstein also does not teach or suggest a method of producing monoclonal antibodies specific to matrix metalloprotease 3 including conjugating the matrix metalloprotease 3 chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 85.

Accordingly, claims 1 and 85 and dependent claims thereof, are patentable over the combination of Seiki and Milstein for at least the reasons described above. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Cashman and Milstein

The Examiner has rejected claims 1, 3, 4, 8-10, 12-14, 16-18, 21, 22, 24, 25, 75 and 81-83 under 35 U.S.C. § 103(a) as being unpatentable over Cashman in view of Milstein. See Office Action at p. 13. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 4, 14, 16-18, 21, 22, 24, 25 and 25 have been cancelled thus rendering this rejection moot with respect to those claims. Claims 3, 8-10 and 12-13 depend from independent claim 1. Claims 81-83 depend from independent claim 75.

As previously described, Cashman does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Cashman also does not teach or suggest a method of producing monoclonal antibodies specific to a Prion protein peptide including conjugating the Prion protein peptide chemically to a carrier molecule wherein the carrier molecule is HSP70 and wherein the prion protein peptide is selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 9 as described in claim 75.

These defects are not remedied by Milstein. Milstein does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Milstein also does not teach or suggest a method of producing monoclonal antibodies specific to a Prion protein peptide including conjugating the Prion protein peptide chemically to a carrier molecule wherein the carrier molecule is HSP70 and wherein the prion protein peptide is selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 9 as described in claim 75.

Accordingly, claims 1 and 75 and dependent claims thereof, are patentable over the combination of Cashman and Milstein for at least the reasons described above. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Cashman and Maurer

The Examiner has rejected claims 1, 3-5, 8-10, 13-25, 75 and 81-83 under 35 U.S.C. § 103(a) as being unpatentable over Cashman in view of Maurer. See Office Action at p. 14. Not

in acquiescence to this rejection but in an effort to expedite prosecution, claims 4 and 14-25 have been cancelled thus rendering this rejection moot with respect to those claims. Claims 3, 5, 8-10 and 13 depend from independent claim 1. Claims 81-83 depend from independent claim 75.

As previously described, Cashman does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Cashman also does not teach or suggest a method of producing monoclonal antibodies specific to a Prion protein peptide including conjugating the Prion protein peptide chemically to a carrier molecule wherein the carrier molecule is HSP70 and wherein the prion protein peptide is selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 9 as described in claim 75.

These defects are not remedied by Maurer. Maurer describes "techniques that have become available for producing antibody ...." See p. 49. Maurer does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Maurer also does not teach or suggest a method of producing monoclonal antibodies specific to a Prion protein peptide including conjugating the Prion protein peptide chemically to a carrier molecule wherein the carrier molecule is HSP70 and wherein the prion protein peptide is selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 9 as described in claim 75.

Accordingly, claims 1 and 75 and dependent claims thereof, are patentable over the combination of Cashman and Maurer for at least the reasons described above. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Seiki and Burnett

The Examiner has rejected claims 1, 3, 4, 6-10, 13, 14, 16-22, 25, 85, 88 and 89 under 35 U.S.C. § 103(a) as being unpatentable over Seiki in view of Burnett et al., "Human Monoclonal Antibodies to Defined Antigens," *In: Human Hybridomas and Monoclonal Antibodies*, Engleman et al., Eds, p. 115 (1985) ("Burnett"). See Office Action at p. 14-15. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 4, 14, 16-22 and 25,

have been cancelled thus rendering this rejection moot with respect to those claims. Claims 3, 6-10 and 13 depend from independent claim 1. Claims 88 and 89 depend from independent claim 85.

As previously described, Seiki does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Seiki also does not teach or suggest a method of producing monoclonal antibodies specific to matrix metalloprotease 3 including conjugating the matrix metalloprotease 3 chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 85.

These defects are not remedied in Burnett. Burnett on p. 115 (as cited by the Examiner) describes "peripheral blood as a source of antigen-primed lymphocytes." Burnett does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Burnett also does not teach or suggest a method of producing monoclonal antibodies specific to matrix metalloprotease 3 including conjugating the matrix metalloprotease 3 chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 85.

Accordingly, claims 1 and 85 and dependent claims thereof, are patentable over the combination of Seiki and Burnett for at least the reasons described above. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Cashman and Lussow

The Examiner has rejected claims 1-4, 8-10, 13-18, 21, 22, 25, 75 and 80-83 under 35 U.S.C. § 103(a) as being unpatentable over Cashman in view of Lussow et al., *European Journal of Immunology*, Vol. 21, pp. 2297-2302 (1991) ("Lussow"). See Office Action at p. 15. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 4, 14-18, 21, 22 and 25 have been cancelled thus rendering this rejection moot with respect to those claims. Claims 2-3, 8-10 and 13 depend from independent claim 1. Claims 81-83 depend from independent claim 75.

As previously described, Cashman does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Cashman also does not teach or suggest a method of producing monoclonal antibodies specific to a Prion protein peptide including conjugating the Prion protein peptide chemically to a carrier molecule wherein the carrier molecule is HSP70 and wherein the prion protein peptide is selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 9 as described in claim 75.

This defect is not remedied by Lussow. Lussow describes the use of mycobacterial heat-shock proteins as carrier molecules in mice previously primed with live BCG. See p. 2300. Lussow further describes that "it was surprising (a) that priming with live BCG was required, and (b) that this in turn, eliminated the need for the use of adjuvants that are normally required when other carrier molecules are utilized." See p. 2301. Lussow is concerned with immunization and development of vaccine strategies. See p. 2301. Lussow does not teach or suggest does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Lussow also does not teach or suggest a method of producing monoclonal antibodies specific to a Prion protein peptide including conjugating the Prion protein peptide chemically to a carrier molecule wherein the carrier molecule is HSP70 and wherein the prion protein peptide is selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 9 as described in claim 75.

Accordingly, claims 1 and 75 and dependent claims thereof, are patentable over the combination of Cashman and Lussow for at least the reasons described above. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Seiki and Lussow

The Examiner has rejected claims 1-4, 6, 8-10, 13-19, 21, 22, 25, 85 and 87-89 under 35 U.S.C. § 103(a) as being unpatentable over Seiki in view of Lussow. See Office Action at p. 15. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 4, 14-19, 21, 22 and 25, have been cancelled thus rendering this rejection moot with respect to those claims.

Claims 2-3, 6, 8-10 and 13 depend from independent claim 1. Claims 87- 89 depend from independent claim 85.

As previously described, Seiki does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Seiki also does not teach or suggest a method of producing monoclonal antibodies specific to matrix metalloprotease 3 including conjugating the matrix metalloprotease 3 chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 85.

This defect is not remedied by Lussow. Lussow describes the use of mycobacterial heat-shock proteins as carrier molecules in mice previously primed with live BCG. See p. 2300. Lussow does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Lussow also does not teach or suggest a method of producing monoclonal antibodies specific to matrix metalloprotease 3 including conjugating the matrix metalloprotease 3 chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 85.

Accordingly, claims 1 and 85 and dependent claims thereof, are patentable over the combination of Seiki and Lussow for at least the reasons described above. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Fillit, Berzofsky, Lussow and Yokoyama

The Examiner has rejected claim 84 under 35 U.S.C. § 103(a) as being unpatentable over Fillit et al., *Journal of Experimental Medicine,* Vol. 164, pp. 762-776 (1986) ("Fillit") in view of Berzofsky et al., *"Antigen-Antibody Interactions and Monoclonal Antibodies," In: Fundamental Immunology,* W.E. Paul, Ed. P. 458 (1993) ("Berzofsky"), Lussow and Yokoyama, *"Production of Monoclonal Antibodies," In: Current Protocols in Immunology*, Unit 2.5 (1991) ("Yokoyama"). See Office Action at p. 16.

Claim 84 relates to a method of producing monoclonal antibodies specific to hyaluronic acid including a) conjugating the hyaluronic acid chemically to a carrier molecule wherein the

carrier molecule is a heat-shock protein, b) immunizing a mammal with the conjugated antigen, c) harvesting B cells from the mammal, d) creating a hybridoma from the harvested B cells and e) screening the hybridomas for specificity to the native hyaluronic acid.

Fillit describes "induction of antibodies to hyaluronic acid by immunization of rabbits with encapsulated streptococci." See Title and Abstract. Fillit does not teach or suggest a method of producing monoclonal antibodies specific to hyaluronic acid that includes conjugating the hyaluronic acid chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein.

This defect is not remedied by Berzofsky, Yokoyama or Lussow. Berzofsky describes the general applications of monoclonal antibodies. See p. 458. Yokoyama describes protocols for production of monoclonal antibodies. Both Berzofsky and Yokoyama do not teach or suggest a method of producing monoclonal antibodies specific to hyaluronic acid that includes conjugating the hyaluronic acid chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein.

As previously explained, Lussow describes the use of mycobacterial heat-shock proteins as carrier molecules in mice previously primed with live BCG. See p. 2300. Lussow further describes that "it was surprising (a) that priming with live BCG was required, and (b) that this in turn, eliminated the need for the use of adjuvants that are normally required when other carrier molecules are utilized." See p. 2301. There is no motivation or suggestion in Lussow or any of the references to modify the teachings of Lussow. As such, Lussow does not teach or suggest a method of producing monoclonal antibodies specific to hyaluronic acid that includes conjugating the hyaluronic acid chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein.

Accordingly, claim 84 is patentable over the combination of Fillit, Berzofsky, Lussow and Yokoyama. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Zatsepina, Lussow and Wu

The Examiner has rejected claims 1-5, 8-10, 13-18, 21, 22, 25, 26, 27, 32-36, 39-42, 45-47, 52-56, 59-62, 65, 73 and 74 under 35 U.S.C. § 103(a) as being unpatentable over Zatsepina,

Yokoyama, Lussow and U.S. Publication No. 2004/0086845 to Wu et al. ("Wu"). See Office Action at p. 17. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 4, 14-18, 21, 22, 25, 34, 46-47, 52-56, 59-62, 65, 73 and 74 have been cancelled thus rendering this rejection moot with respect to those claims. Claims 2-3, 5, 8-10 and 13 depend from independent claim 1. Claims 27, 32-33, 35-36, 39-42 and 45 depend from independent claim 26.

Claim 1 relates to a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including a) conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein, b) immunizing a mammal with the conjugated antigen, c) harvesting B cells from the mammal, d) creating hybridomas from the harvested B cells, e) screening the hybridomas for specificity to the native antigen. Claim 26 relates to a method of producing monoclonal antibodies specific to E7 oncoprotein including a) conjugating the E7 oncoprotein chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein, b) immunizing a mammal with the conjugated antigen, c) harvesting B cells from the mammal, d) creating a hybridoma from the harvested B cells, and e) screening the hybridomas for specificity to the native E7 oncoprotein.

Zatsepina describes the generation of HPV16 E7 monoclonal antibodies. See p. 1138. Zatsepina does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity that includes conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein. Zatsepina further does not teach or suggest a method of producing monoclonal antibodies specific to E7 oncoprotein including conjugating the E7 oncoprotein chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein.

These defects are not remedied by the other references. Yokoyama describes protocols for production of monoclonal antibodies. Yokoyama does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity that includes conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein. Yokoyama further does not teach or suggest a method of producing monoclonal antibodies specific to E7 oncoprotein including conjugating the E7 oncoprotein chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein.

Wu describes "[n]ucleic acids encoding a chimeric or fusion polypeptide which polypeptide comprises a first domain comprising a translocation polypeptide; and a second domain comprising at least one antigenic peptide ...." See Abstract. Wu does not teach or suggest method of producing monoclonal antibodies specific to an antigen of low immunogenicity that includes conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein. Wu further does not teach or suggest a method of producing monoclonal antibodies specific to E7 oncoprotein including conjugating the E7 oncoprotein chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein.

As previously explained, Lussow describes the use of mycobacterial heat-shock proteins as carrier molecules in mice previously primed with live BCG. See p. 2300. Lussow further describes that "it was surprising (a) that priming with live BCG was required, and (b) that this in turn, eliminated the need for the use of adjuvants that are normally required when other carrier molecules are utilized." See p. 2301. As such, there is no motivation or suggestion in Lussow or any of the references to modify the teachings of Lussow. Accordingly, Lussow does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity that includes conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein. Lussow also does not teach or suggest a method of producing monoclonal antibodies specific to E7 oncoprotein including conjugating the E7 oncoprotein chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein.

Accordingly, claims 1, 26 and dependent claims thereof are patentable over the combination of Zatsepina, Lussow, Yokoyama and Wu. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Zatsepina, Lussow, Wu, Yokoyama and Seiki

The Examiner has rejected claims 1-6, 8-10, 13-19, 21, 22, 25, 26, 27, 32-37, 39-42, 45-47, 52-57, 59-62, 65, 73 and 74 under 35 U.S.C. § 103(a) as being unpatentable over Zatsepina, Lussow, Wu and Yokoyama and further in view of Seiki. See Office Action at p. 18. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 4, 14-19, 21, 22, 25,

34, 46-47, 52-57, 59-62, 65, 73 and 74 have been cancelled thus rendering this rejection moot with respect to those claims. Claims 2-3, 5, 8-10 and 13 depend from independent claim 1. Claims 27, 32-33, 35-37, 39-42 and 45 depend from independent claim 26.

As previously explained, Zatsepina, Lussow, Wu and Yokoyama, alone or in combination, do not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity that includes conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Zatsepina, Lussow, Wu and Yokoyama, alone or in combination, also do not teach or suggest a method of producing monoclonal antibodies specific to E7 oncoprotein including conjugating the E7 oncoprotein chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 26.

Seiki describes methods of making a monoclonal antibody to human MT-MMP-3 and further describes that fragment so MT-MMP-3 "be coupled with various carrier proteins via suitable coupling agents to form immunogenic conjugates such as hapten-proteins." See col. 18, lines 27-36 and col. 18, line 63 to col. 19, line 3. Seiki further states that "[t]he carrier proteins include keyhole limpet haemocyanin (KLH), bovine serum albumin (BSA), ovalbumin, globulin, polypeptides such as polylysine, bacterial components such as BCG or the like." See col. 19, lines 15-18. Seiki does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity that includes conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Seiki further does not teach or suggest a method of producing monoclonal antibodies specific to E7 oncoprotein including conjugating the E7 oncoprotein chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 26.

Accordingly, claims 1, 26 and dependent claims thereof are patentable over the combination of Zatsepina, Lussow, Yokoyama, Wu and Seiki. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Zatsepina, Lussow, Wu, Yokoyama and Burnett

The Examiner has rejected claims 1-5, 7-10, 13-18, 20-22, 25, 26, 27, 32-36, 38-42, 45-47, 52-56, 58-62, 65, 73 and 74 under 35 U.S.C. § 103(a) as being unpatentable over Zatsepina,

Lussow, Wu and Yokoyama and further in view of Burnett. See Office Action at p. 18. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 4, 14-18, 20-22, 25, 34, 46-47, 52-56, 58-62, 65, 73 and 74 have been cancelled thus rendering this rejection moot with respect to those claims. Claims 2-3, 5, 7-10 and 13 depend from independent claim 1. Claims 27, 32-33, 35-36, 38-42 and 45 depend from independent claim 26.

As previously explained, Zatsepina, Lussow, Wu and Yokoyama, alone or in combination, do not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity that includes conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Zatsepina, Lussow, Wu and Yokoyama, alone or in combination, also do not teach or suggest a method of producing monoclonal antibodies specific to E7 oncoprotein including conjugating the E7 oncoprotein chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 26.

These defects are not remedied in Burnett. Burnett on p. 115 (as cited by the Examiner) describes "peripheral blood as a source of antigen-primed lymphocytes." Burnett does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Burnett further does not teach or suggest a method of producing monoclonal antibodies specific to E7 oncoprotein including conjugating the E7 oncoprotein chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 26.

Accordingly, claims 1, 26 and dependent claims thereof are patentable over the combination of Zatsepina, Lussow, Yokoyama, Wu and Burnett. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Zatsepina, Lussow, Wu, Yokoyama and Zwerschke

The Examiner has rejected claims 1-5, 8-10, 13-18, 21, 22, 25, 26, 27, 31-36, 39-42, 45-47, 51-56, 59-62, 65, 73 and 74 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Zatsepina, Lussow, Wu and Yokoyama and further in view of Zwerschke. See Office Action at p. 19. Not in acquiescence to this rejection but in an effort to expedite

prosecution, claims 4, 14-18, 21, 22, 25, 34, 46-47, 51-56, 59-62, 65, 73 and 74 have been cancelled thus rendering this rejection moot with respect to those claims. Claims 2-3, 5, 8-10 and 13 depend from independent claim 1. Claims 27, 31-33, 35-36, 39-42 and 45 depend from independent claim 26.

As previously explained, Zatsepina, Lussow, Wu and Yokoyama, alone or in combination, do not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity that includes conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Zatsepina, Lussow, Wu and Yokoyama, alone or in combination, also do not teach or suggest a method of producing monoclonal antibodies specific to E7 oncoprotein including conjugating the E7 oncoprotein chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 26.

These defects are not remedied in Zwerschke. Zwerschke describes "an anti-HPV-16 E7 antibody obtainable by (a) eliciting an in vivo humoral response against highly purified HPV-16 E7 protein or a fragment thereof in a non-human vertebrate ...." See Abstract. Zwerschke does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity that includes conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Zwerschke also does not teach or suggest a method of producing monoclonal antibodies specific to E7 oncoprotein including conjugating the E7 oncoprotein chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 26.

Accordingly, claims 1, 26 and dependent claims thereof are patentable over the combination of Zatsepina, Lussow, Yokoyama, Wu and Zwerschke. Applicants respectfully request reconsideration and the withdrawal of this rejection.

Zatsepina, Lussow, Wu, Yokoyama and Milstein

The Examiner has rejected claims 1-5, 8-10, 12-18, 21, 22, 24-27, 32-36, 39-42, 44-47, 52-56, 59-62, 64, 65, 73 and 74 under 35 U.S.C. § 103(a) as being unpatentable over Zatsepina, Lussow, Wu and Yokoyama and further in view of Milstein. See Office Action at p. 19. Not in acquiescence to this rejection but in an effort to expedite prosecution, claims 4, 14-18, 21, 22,

24-25, 34, 46-47, 52-56, 59-62, 64, 65, 73 and 74 have been cancelled thus rendering this rejection moot with respect to those claims. Claims 2-3, 5, 8-10 and 12-13 depend from independent claim 1. Claims 27, 32-33, 35-36, 39-42 and 44-45 depend from independent claim 26.

As previously explained, Zatsepina, Lussow, Wu and Yokoyama, alone or in combination, do not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity that includes conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Zatsepina, Lussow, Wu and Yokoyama, alone or in combination, also do not teach or suggest a method of producing monoclonal antibodies specific to E7 oncoprotein including conjugating the E7 oncoprotein chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 26.

These defects are not remedied by Milstein. As explained by the Examiner, Milstein describes "that hybridomas can be made by fusing rat or mouse spleen cells with rat myeloma cells." See Office Action at p. 20. Milstein does not teach or suggest a method of producing monoclonal antibodies specific to an antigen of low immunogenicity including conjugating the antigen chemically to a carrier molecule, wherein the carrier molecule is a heat-shock protein as described in claim 1. Milstein also does not teach or suggest a method of producing monoclonal antibodies specific to E7 oncoprotein including conjugating the E7 oncoprotein chemically to a carrier molecule wherein the carrier molecule is a heat-shock protein as described in claim 26.

Accordingly, claims 1, 26 and dependent claims thereof are patentable over the combination of Zatsepina, Lussow, Yokoyama, Wu and Milstein. Applicants respectfully request reconsideration and the withdrawal of this rejection.

CONCLUSION

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the claims now pending are in condition for allowance.

Should any fees be required by the present Amendment, the Commissioner is hereby authorized to charge Deposit Account **19-4293**.

Respectfully submitted,

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